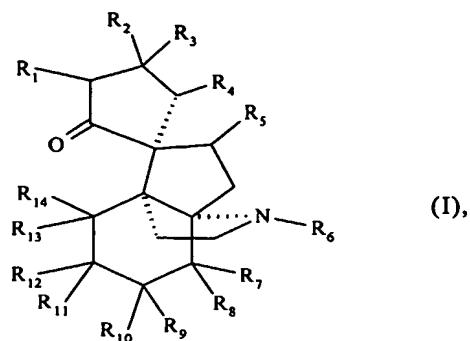


CLAIMS

1. Compounds of formula (I) :



wherein

- R₁ and R₂ each represent a hydrogen atom or together form an additional bond,
- R₃ represents a hydrogen atom or an alkoxy group,
- R₄ represents a hydrogen atom or a hydroxy, alkoxy, alkylcarbonyloxy or arylcarbonyloxy group,
- R₅ represents a hydrogen or halogen atom,
- R₆ represents a hydrogen atom or an alkyl, alkylcarbonyl or aroyl group,
- R₇ represents an alkoxy group,
- R₈ and R₉ together form an additional bond,
or R₈ and R₁₃ together form a sulphide bridge and, in that case, R₉ and R₁₀ together form an oxo group and R₁₄ represents a chlorine atom,
- R₁₀ represents an alkoxy group,
- R₁₁ represents a hydroxy or alkoxy group,
- R₁₂ represents a hydrogen atom,
or R₁₁ and R₁₂ together form an oxo, oxime or O-alkyl-oxime group,
- and R₁₃ and R₁₄ each represent a hydrogen atom or together form an oxo group,

with the proviso that the compound of formula (I) cannot represent :

- spiro[(4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one] (acutumine)
- 5 - spiro[(4S,5S)-4-acetyl-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one]
- spiro[(4S,5S)-4-acetyl-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-acetylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one]
- 10 - spiro[(4S,5S)-4-(benzoyloxy)-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one]
- spiro[(4S,5S)-4-hydroxy-cyclopentan-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-ol]
- 15 - spiro[(4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one]
- spiro[(4R,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one]
- 20 - spiro[(4S,5S)-4(benzoyloxy)-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1benzoylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one]
- spiro[(4S,5S)-4-acetyl-cyclopentan-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one]
- 25 - spiro[4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1*H*-pyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one] (acutumidine)
- spiro[4R,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1*H*-pyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one]
- spiro[(5S)-2-methoxy-2-cyclopenten-1-one-5:3-3aS,7aS-((2,3)-1*H*-pyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one]
- 30 - spiro[(5S)-2-methoxy-2-cyclopenten-1-one-5:3-2-chloro-3aS,7aS-((2,3)-1*H*-pyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one],

it being understood that

- "alkyl" means an alkyl group containing 1 to 6 carbon atoms which may be linear or branched,
- "alkoxy" means an alkyloxy group containing 1 to 6 carbon atoms which may be linear or branched,
- "aryloxy" means an aryloxy group wherein the aryl moiety represents a phenyl or naphthyl group,
- "aroyl" means an arylcarbonyl group wherein the aryl moiety represents a phenyl or naphthyl group,

5

10 their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

15

2. Compounds of formula (I) according to claim 1, wherein R₁ and R₂, on the one hand, and R₈ and R₉, on the other hand, together form an additional bond, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

3. Compounds of formula (I) according to claim 1, wherein the groups R₃, R₇ and R₁₀ each represent a methoxy group, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

20

4. Compounds of formula (I) according to claim 1, wherein R₄ represents a hydroxy, acyloxy or benzyloxy group, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

5. Compounds of formula (I) according to claim 1, wherein R₅ represents a chlorine atom, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

25

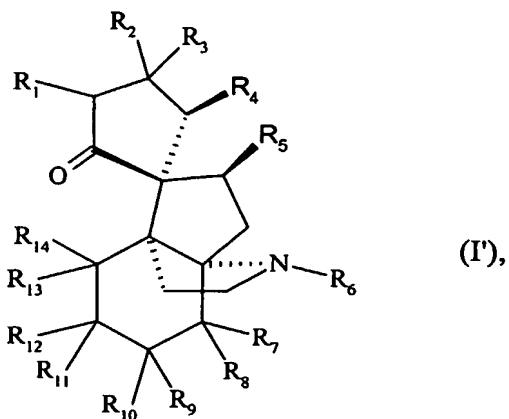
6. Compounds of formula (I) according to claim 1, wherein R₆ represents a methyl or ethyl group, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

7. Compounds of formula (I) according to claim 1, wherein R₆ represents a hydrogen atom, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

5 8. Compounds of formula (I) according to claim 1, wherein R₁₁ and R₁₂ together form an oxo group, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

9. Compounds of formula (I) according to claim 1, wherein R₁₃ and R₁₄ each represent a hydrogen atom, their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

10. Compounds of formula (I) according to claim 1, having the configuration shown by formula (I') :

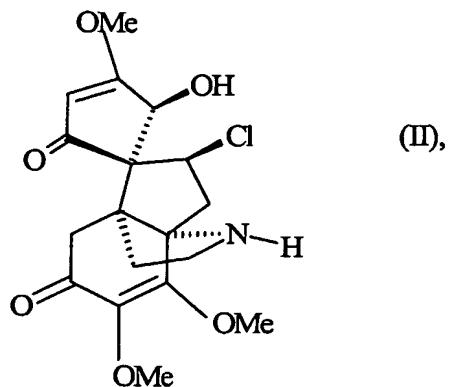


their enantiomers and diastereoisomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

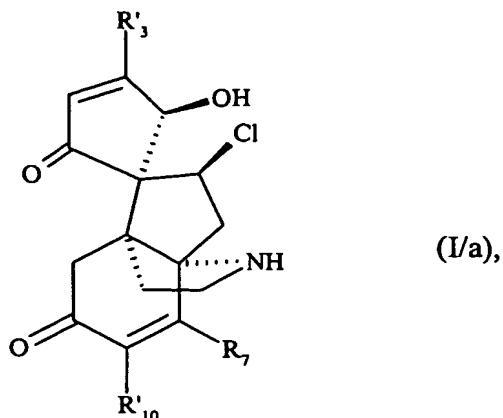
15 11. Compounds of formula (I) according to claim 1, which are spiro[(4S,5S)-4-(ethoxycarbonyl)-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], spiro[(4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-ethyl-pyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], spiro[(4S,5S)-4-(ethoxycarbonyl)-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-

3aS,7aS-((2,3)-1-propanoylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], spiro[(4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one oxime], spiro[(4S,5S)-3,4-dimethoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one],
5 spiro[(4R,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-2,3,3a,7a-tetrahydro-4H,5H-indene-4,5-dione], spiro[(5S)-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], spiro[(4S,5S)-4-hydroxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-ol], spiro[(4R,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2,4-dichloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-7-methoxy-8-thiabicyclo[2.2.1]-1,2,3,3a,4,7a-hexahydro-5H,6H-indene-5,6-dione], their enantiomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

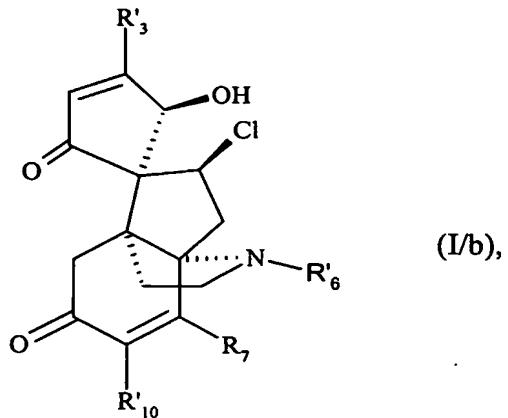
15 12. Process for the preparation of compounds of formula (I) according to claim 1, characterised in that there is used as starting material the compound of formula (II) :



which is subjected to the action of, successively, a demethylating agent and then an alkylating agent to obtain the compound of formula (I/a), a particular case of the compounds of formula (I) :

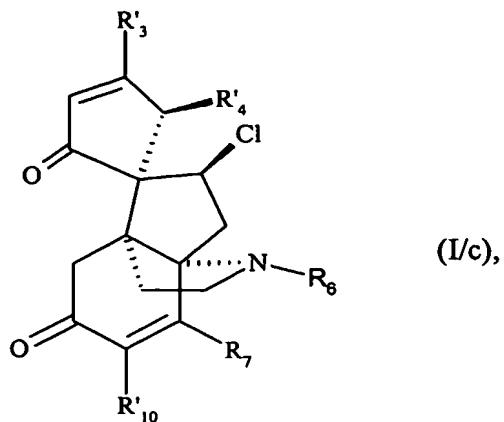


wherein R'3 and R'10 each represent an alkoxy group and R7 is as defined for formula (I), which may be subjected to the action of a compound of formula R₁₅CHO (wherein R₁₅ represents an alkyl group) in a reducing medium to obtain the compound of formula (I/b), a particular case of the compounds of formula (I) :



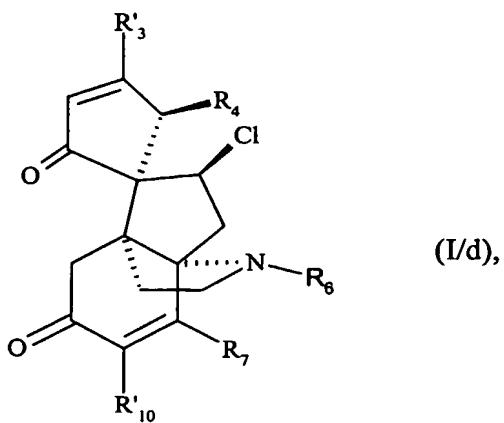
wherein R'3, R7 and R'10 are as defined hereinbefore and R'6 represents an alkyl group,

which compounds of formula (II), (I/a) or (I/b) may be subjected to the action of a compound of formula (R₁₆CO)₂O (wherein R₁₆ represents an alkyl or aryl group) to yield the compound of formula (I/c), a particular case of the compounds of formula (I) :



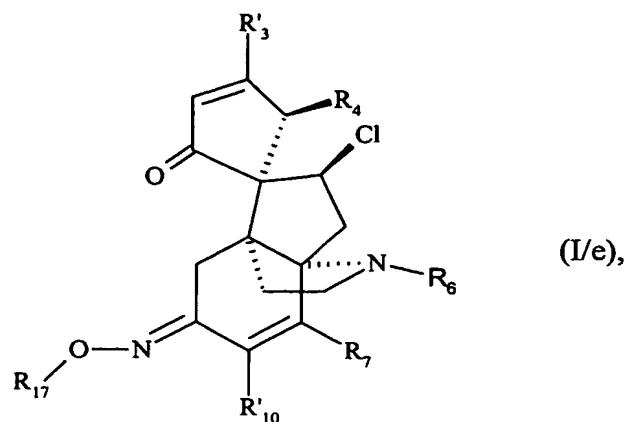
wherein R'₃, R₇ and R'₁₀ are as defined hereinbefore, R₆ is as defined for formula (I) and R'₄ represents a hydroxy, alkylcarbonyloxy or arylcarbonyloxy group,

or which compounds of formula (II), (I/a), (I/b) or (I/c) may be subjected to the action of a compound of formula E-R₁₅ (wherein R₁₅ represents an alkyl group and E represents a leaving group such as a halogen atom or a tosyl group) to yield the compound of formula (I/d), a particular case of the compounds of formula (I) :

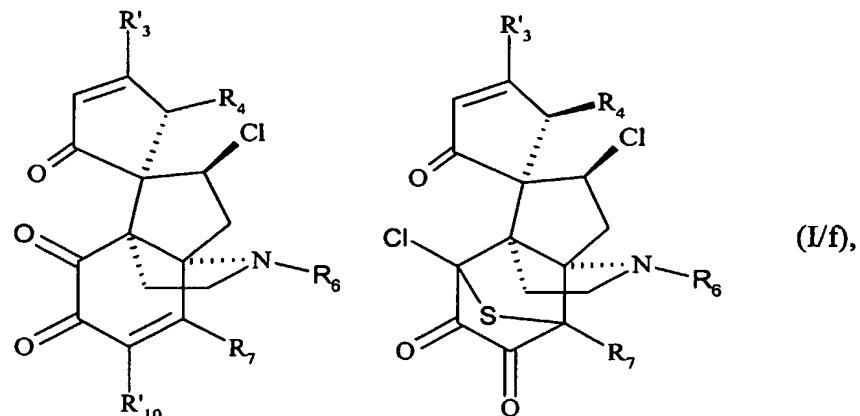


wherein R'₃, R₆, R₇ and R'₁₀ are as defined hereinbefore and R₄ is as defined for formula (I),

which may be subjected to the action of the compound of formula R₁₇ONH₂ wherein R₁₇ represents a hydrogen atom or an alkyl group to yield the compound of formula (I/e), a particular case of the compounds of formula (I) :



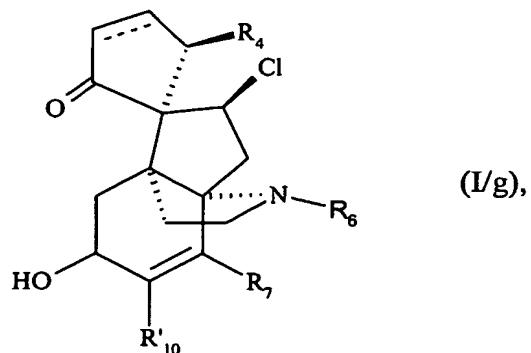
wherein R'₃, R₄, R₆, R₇, R'₁₀ and R₁₇ are as defined hereinbefore,
or which compound of formula (I/d) may be subjected to the action of SOCl₂/DMF to obtain
the compounds of formula (I/f), particular cases of the compounds of formula (I) :



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wherein R'₃, R₄, R₆, R₇ and R'₁₀ are as defined hereinbefore,

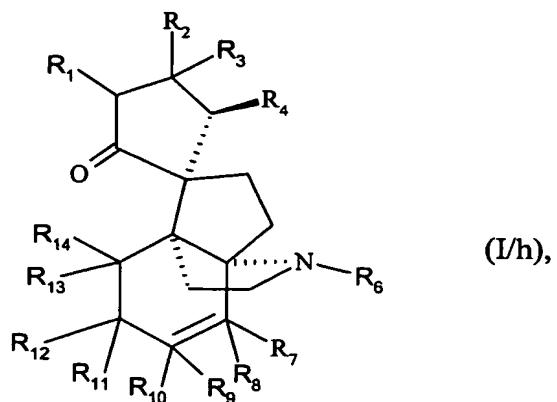
or which compound of formula (I/d) may be subjected to the action of a reducing agent such as LiAlH₄ to obtain the compounds of formula (I/g), particular cases of the compounds of formula (I) :



10

wherein R₄, R₆, R₇ and R'₁₀ are as defined hereinbefore and the symbol ----- indicates that the bond may be single or double,

5 or which compound of formula (I/d), (I/e), (I/f) or (I/g) may be subjected to the action of n-Bu₃SnH in the presence of AIBN to obtain the compounds of formula (I/h), particular cases of the compounds of formula (I) :



wherein R₄, R₆ and R₇ are as defined hereinbefore and R₁, R₂, R₃, R₅, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₃ and R₁₄ are as defined for formula (I),

10 the compounds of formulae (I/a) to (I/h) constituting the totality of the compounds of the invention, which may be purified according to a conventional separation technique, are converted, if desired, into their addition salts with a pharmaceutically acceptable acid or base and are separated, where appropriate, into their isomers according to a conventional separation technique.

15 13. Pharmaceutical compositions comprising at least one compound of formula (I) according to any one of claims 1 to 11 or an addition salt thereof with a pharmaceutically acceptable acid or base, in combination with one or more pharmaceutically acceptable excipients.

20 14. Pharmaceutical compositions according to claim 13 for use in the manufacture of medicaments for the treatment of deficiencies of memory associated with cerebral ageing and with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Pick's disease, Korsakoff's disease, and frontal lobe and subcortical dementias.

15. Use of acutumine and/or acutumine compounds in obtaining pharmaceutical compositions intended for the treatment of deficiencies of memory associated with cerebral ageing and with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Pick's disease, Korsakoff's disease, and frontal lobe and subcortical dementias.

5 **16. Use, according to claim 15, of acutumine in obtaining pharmaceutical compositions intended for the treatment of deficiencies of memory associated with cerebral ageing and with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Pick's disease, Korsakoff's disease, and frontal lobe and subcortical dementias.**

17. Use, according to claim 15, of acutumine compounds in obtaining pharmaceutical compositions intended for the treatment of deficiencies of memory associated with cerebral ageing and with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Pick's disease, Korsakoff's disease, and frontal lobe and subcortical dementias.

18. Use, according to claim 15, of spiro[(4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one] (acutumine), of spiro[(4S,5S)-4-acetyl-3-methoxy-2-

15 **cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], of spiro[(4S,5S)-4-acetyl-3-methoxy-2-**

cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-acetylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], of spiro[(4S,5S)-4-(benzoyloxy)-3-methoxy-2-

cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], of spiro[(4S,5S)-4-hydroxy-cyclopentan-1-one-

5:3(2S)-2-chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], of spiro[(4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-

5:3(2S)-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-

inden-5-one], of spiro[(4R,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-

chloro-3aS,7aS-((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-

inden-5-one], of spiro[(4S,5S)-4(benzoyloxy)-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-

chloro-3aS,7aS-((2,3)-1benzoylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-

inden-5-one], of spiro[(4S,5S)-4-acetyl-cyclopentan-1-one-5:3(2S)-2-chloro-3aS,7aS-

25 **((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], of spiro[4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-**

((2,3)-1-methylpyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5H-inden-5-one], of spiro[4S,5S)-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2S)-2-chloro-3aS,7aS-

1*H*-pyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one] (acutumidine),
of spiro[4*R*,5*S*]-4-hydroxy-3-methoxy-2-cyclopenten-1-one-5:3(2*S*)-2-chloro-3a*S*,7a*S*-
(*2,3*)-1*H*-pyrrolidine)-6,7-dimethoxy-1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one], of
spiro[(5*S*)-2-methoxy-2-cyclopenten-1-one-5:3-3a*S*,7a*S*-((*2,3*)-1*H*-pyrrolidine)-6,7-
dimethoxy-1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one], or of spiro [(5*S*)-2-methoxy-2-
cyclopenten-1-one-5:3-2-chloro-3a*S*,7a*S*-((*2,3*)-1*H*-pyrrolidine)-6,7-dimethoxy-
1,2,3,3a,4,7a-hexahydro-5*H*-inden-5-one]

5

in obtaining pharmaceutical compositions intended for the treatment of deficiencies of memory
associated with cerebral ageing and with neurodegenerative diseases such as Alzheimer's
10 disease, Parkinson's disease, Pick's disease, Korsakoff's disease, and frontal lobe and
subcortical dementias.

10

19. Pharmaceutical compositions comprising acutumine or an acutumine compound, in
combination with one or more pharmaceutically acceptable excipients, for use in the
treatment of deficiencies of memory associated with cerebral ageing and with

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neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Pick's
disease, Korsakoff's disease, and frontal lobe and subcortical dementias.